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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Clare Passmore et al.

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For: Topical Compositions

Group A.U.: 1615

I hereby certify that this paper is being deposited this date with the U.S. Postal Service in first class mail addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

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Date 7.14.00

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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

As a means of complying with the duty of disclosure set forth in 37 CFR § 1.56 and in keeping with the guidelines of 37 CFR § 1.98, Applicants hereby submit information thought to be relevant to the above-identified application. Also submitted herewith is a completed form PTO-1449.

Supplemental to the Information Disclosure Statement submitted on June 7, 2000, Applicants submit an additional reference thought to be relevant to the above identified application.

This information came to light during examination of a counterpart PCT Application in the European Patent Office in an International Search Report dated August 10, 1998.

No Office Action on the merits has been mailed to the

knowledge of the Applicants or Applicants' undersigned.

Drug Release Studies On Oil-Water Emulsion Based On a Eutectic Mixture of Lidocaine and Prilocaine As the Dispersed Phase, Nyquist-Mayer et al., Journal of Pharmaceutical sciences, Vol. 75, No.4, April 1996, Pages 365-373 apparently relates to an experiment wherein in vitro drug release properties of a topical anesthetic formulation based upon a 1:1 eutectic mixture of lidocaine and prilocaine emulsified in water were investigated with a poly (dimethylsiloxane) membrane partition model. Aqueous solutions and solubilized systems of lidocaine and prilocaine in a 1:1 ratio by weight were also included in the study. Two identical sets of samples were used, one of which was gelled with carbomer 934 P. Thereafter, drug solubilities in the membrane, partition coefficients between membrane and water, and the diffusion coefficients in the membrane and the formulations were determined. The results indicated that lidocaine and prilocaine in combination had lower solubilities in the membrane than they did separately. However, in the aqueous phase or in the membrane, the diffusion coefficients were mutually independent. Moreover, carbomer 934 P, when neutralized totally with sodium hydroxide, did not decrease the aqueous diffusivities of the local anesthetic bases. Therefore, the major advantages of using the emulsion formulation based on a eutectic mixture rather than the more conventional formulations were: the local anesthetic bases were present in their permeable unchanged forms; the use of a poor solvent like water as the vehicle provided a saturated system at

poor concentrations; lipophilic solvent was absent in the dispersed phase; the droplets consisted of a dissolvable drug and acted as reservoirs in order to obtain steady-state release; and, the fluid state of the excess drug provided a higher dissolution rate than from a solid state.

No fee is deemed necessary in connection with the filing of this Supplemental Information Disclosure Statement. However, if a fee is required for this submission, the Commissioner is authorized to charge the requisite fee to Deposit Account No. 03-3125.

Respectfully submitted,

COOPER & DUNHAM LLP

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JHM/DRM
Encl.